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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,358	PIEPER ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 27, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,52,62-69,84,85,88,89 and 104-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,52,62-69,84,85,88,89 and 104-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *December 27, 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because:

> It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.
>
> It does not identify the U.S. provisional application on which priority is claimed.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Specifically, the specification does not appear to provide antecedent basis for the language "specific predefined proteins" as recited in claims 63 and 84. Correction is required.

Claim Rejections - 35 USC § 112

Claims 32, 52, 62-69, 84-85, 88-89 and 104-107 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 63 and 84, the recitation of "specific predefined proteins" is indefinite and lacks antecedent support in the specification.

In claim 63, the recitation of "solid phase matrices" lacks antecedent basis and is indefinite. Whether "solid phase matrices" references "a first and second solid phase matrix" is not clear.

In claims 63 and 84, the recitation of "each solid phase matrix comprises a plurality of particles" is indefinite, wherein "each solid phase matrix" = a bead (see specification p. 9, lines 10-11, "[a] suitable matrix is, for example a bead or a microbead shape") (emphases added). Whether/how a bead comprises "a plurality of particles" is not clear.

In claim 63, the recitation of "a first and second solid phase matrix contacting each other" is indefinite, wherein "each solid phase matrix" = beads (see specification p. 13, lines 4-7, "the matrix is loose beads... matrix beads") (emphases added). Whether/how a matrix of beads is in contact with another matrix of beads is not clear. Whether the claim limitation "contacting" requires a matrix of beads to be stacked, layered and/or adjoined on/to another matrix of beads is not clear. How a matrix of beads that is stacked, layered and/or adjoined on/to another matrix of beads can be "present as a mixture" is not clear.

In claim 84, the recitation of "each solid phase matrix is in contact with at least one other solid phase matrix" is indefinite, wherein "each solid phase matrix" = beads (see specification p. 13, lines 4-7, "the matrix is loose beads... matrix beads") (emphases added). Whether/how a matrix of beads is in contact

with another matrix of beads is not clear. Whether the claim limitation "in contact" requires a matrix of beads to be stacked, layered and/or adjoined on/to another matrix of beads is not clear. How a matrix of beads that is stacked, layered and/or adjoined on/to another matrix of beads can be present "as a mixture" is not clear.

Claim Rejections - 35 USC § 102

Claims 32, 52, 62-69, 84, 89 and 104 are rejected under 35 U.S.C. 102(b) as being anticipated by Brian et al., 391 FEBS LETTERS 71 (1996).

Brian et al. describe a method for separating proteins (see Fig. 1, "scFv antibody library") from a sample that contains proteins (see p. 72, col. 1, third paragraph, "cytosolic cell extracts") and recovering a modified sample (see Abstract, "enrich selectively phage displayed antibodies directed against proteins constituting a difference between two populations of cells") comprising the steps of: removing (see p. 72, col. 1, fifth paragraph, "immunobead was washed", see Fig. 2(A), MIX+LDH versus MIX) at least two specific predefined proteins (see p. 73, col. 2, second paragraph, "Competitive proteins were... also added in solution", see Fig. 2(A), MIX+LDH versus MIX), recovering the modified sample (see Abstract, "enrich selectively phage displayed antibodies directed against proteins constituting a difference between two populations of cells"), wherein the removing step comprises contacting the sample with an affinity binding composition (see Fig. 1, "two solid phase system") comprising a first and second solid phase matrix (see Fig. 1, "two solid phase system") contacting each other (see Fig. 1, "immunobeads in an immunotube"), wherein each solid phase matrix comprises a plurality of particles (see Fig. 1, "immunobeads in an immunotube"), wherein the particles are present in a mixture (see p. 72, col. 1, sixth paragraph, "4 ml 2% MPBS... five immunobeads... were added"), a first receptor (see Fig. 1, "LDH") immobilized on said first solid phase matrix (see Fig. 1, "immunobeads), and a second receptor (see Fig. 1, "MIX proteins") immobilized on said second solid phase matrix (see Fig. 1, "immunotube").

With respect to claims 64-69, Brian et al. describe a method wherein "different coating conditions in parallel" is performed "to cover as many proteins as possible" (see p. 74, col. 2, second full paragraph, last sentence).

Claims 32, 52, 62-69, 84, 88-89 and 104 are rejected under 35 U.S.C. 102(e) as being anticipated by Payan (US 6,455,263).

Payan describes a method for separating proteins (see col. 13, lines 1-2, "beads are then sorted using fluorescent-activated cell sorting") from a sample that contains proteins (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules") and recovering a modified sample (see col. 2, lines 64-65, "collected") comprising the steps: removing at least two specific predefined proteins (see *e.g.*, col. 13, lines 10-11, "non-fluorescent beads") from a sample that contains the at least two specific predefined proteins (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules"), thereby producing a modified sample containing a plurality of proteins (see col. 13, lines 10-11, "sorting results in a population of non-fluorescent beads and at least one population of fluorescent beads"), recovering the modified sample (see col. 2, lines 64-65, "collected"), wherein the removing step comprises contacting the sample with an affinity binding composition (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules") comprising: a first and second solid phase matrix contacting each other, wherein each solid phase matrix comprises a plurality of particles (see col. 7, line 52, "bead composition"), and wherein the particles are present as a mixture (see col. 12, line 55, "reaction mixture").

With respect to claims 88 and 104, Payan describes antibody candidate agents (see col. 9, lines 39-42).

With respect to claim 89, Payan describes libraries of synthetic compounds and their generation (see col. 3, lines 51-65).

Claim Rejections - 35 USC § 103

Claims 32, 52, 62-69, 84-85, 88-89 and 104-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davies (US 6,696,304) in view of Payan (US 6,455,263).

Davies describes a method for separating proteins (see col. 16, line 67, "screening of combinatorial libraries") comprising the step of contacting a sample with an affinity binding composition (see col. 9, lines 48-50, "[a] test analyte/microparticle complex is added directly to the mixture of microparticles with immobilized protein standards") comprising: a plurality of solid phase matrices (see Title, "particulate solid phase") arranged such that each solid phase matrix is in contact with at least one other solid phase matrix (see col. 9, lines 48-50, "[a] test analyte/microparticle complex is added directly to the mixture of microparticles with immobilized protein standards"), and wherein each solid phase matrix (see col. 9, line 48, "[a] test analyte/microparticle complex"; col. 9, lines 49-50, "mixture of microparticles with immobilized protein standards") comprises a plurality of particles, and wherein the pluralities of particles are present as a mixture (see col. 9, lines 48-49, "added directly to the mixture"); and a plurality of receptors immobilized on the plurality of solid phase matrices (see *e.g.*, col. 14, line 52, "antibody").

Davies does not describe the steps of "removing at least two specific predefined proteins from a sample", "producing a modified sample" and "recovering the modified sample".

However, Payan describes a method for separating proteins (see col. 13, lines 1-2, "beads are then sorted using fluorescent-activated cell sorting") and recovering a modified sample (see col. 2, lines 64-65, "collected") comprising the steps: removing at least two specific predefined proteins (see *e.g.*, col. 13, lines 10-11, "non-fluorescent beads") from a sample that contains the at least two specific predefined proteins (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules"), thereby producing a modified sample containing a plurality of proteins

(see col. 13, lines 10-11, "sorting results in a population of non-fluorescent beads and at least one population of fluorescent beads"), recovering the modified sample (see col. 2, lines 64-65, "collected").

Therefore, it would have been obvious for a person of ordinary skill in the art to perform the method for screening combinatorial libraries of Davies with the added procedural steps of producing and recovering a modified sample because Payan discovered that producing and recovering a modified sample using FACS allows for subsequent analysis (see col. 2, line 65), treatment (see col. 3, line 8) and/or characterization (see col. 3, line 10) of separated proteins.

With respect to claim 85, Davies describes an affinity purification column containing the affinity binding composition (see col. 17, lines 47-48, "affinity purification columns").

With respect to claims 104-107, Davies describes an affinity binding composition that binds to albumin (see col. 15, line 9), immunoglobulins (see col. 15, lines 16-19), transferrin (see col. 15, line 16), haptoglobin (see col. 15, line 15), alpha-1-antitrypsin (see col. 15, line 12), alpha-2-macroglobulin (see col. 15, line 12), alpha-1-acid glycoprotein (see col. 15, line 9), hemopexin (see col. 15, line 15), transthyretin (see col. 15, line 14), apolipoprotein A1 (see col. 15, line 13) and prealbumin (see col. 15, line 14).

Response to Arguments

In prior Office Action, claims 32, 52, 62-69, 84, 89 and 104 were rejected under 35 U.S.C. 102(b) as being anticipated by Brian *et al.*, 391 FEBS LETTERS 71 (1996). In response, Applicants argue:

1. Brian *et al.* teach removal of one phage, whereas the instant invention requires removal of two proteins (see Applicants' reply, p. 7, fourth paragraph, "there is no indication that any proteins bound to the immunobeads"; "it is entirely unclear which proteins, if any, may have bound"; "Brian does not indicate that the phage that bound to the immunobeads did in fact display at least two different antibodies"; p. 8, first full paragraph, "Brian teaches recovery of phage").
2. Brian *et al.* do not teach a step of characterizing antibodies (see Applicants' reply, p. 8, lines 5-6, "he [Brian] does not characterize the antibodies that bound to LDH").
3. Brian's *et al.* description of "immunobeads" does not amount to a "first and second solid phase matrix" (see Applicants' reply, p. 8, second full paragraph, "the immunobeads are not first and second solid phase matrices").

Applicants' arguments have been carefully considered but are not persuasive.

With respect to argument 1), *supra*, Examiner observes that Applicants' argument appears to rely upon a specific set of experiments performed by Brian *et al.* and the specific data obtained therefor. Applicants' argument does not appear to give deference to the broader analytical framework established by Brian *et al.,* namely, the analysis of differential gene expression (see Title, "A model phage display substraction method with potential for analysis of differential gene expression") (emphasis added).

According to MPEP 2123, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments.

Examiner posits that persons of ordinary skill, upon a thorough reading and understanding of the teachings of Brian *et al.,* would conclude that the broader analytical framework established by Brian *et al.* was not to isolate a single phage antibody against LDH, but rather to establish a model system (see Title, "A model phage display subtraction method"; see p. 71, col. 2, last paragraph, "[a] competitive biopanning

procedure was developed and tested on two model systems") to be used for isolating multiple phage antibodies against differentially expressed proteins (see p. 71, col. 2, last paragraph, "the subtractive strategy presented is valuable in attempts to identify antibodies against known or unknown antigens in a given population of cells", noting Brian's *et al.* use of plural "antibodies" and "antigens").

With respect to argument 2), *supra*, Applicants' observation is noted.

With respect to argument 3), *supra*, Brian's *et al.* description of "immunobeads" (plural) reads on a "first and second solid phase matrix", wherein "solid phase matrix" = a bead (see specification p. 9, lines 10-11, "[a] suitable matrix is, for example a bead or a microbead shape") (emphases added).

In prior Office Action, claims 32, 52, 62-69, 84-85, 88-89 and 104 were rejected under 35 U.S.C. 102(b) as being anticipated by Rubenstein (US 5,879,881). In addition, claims 32, 52, 62-69, 84-85, 88-89 and 104-107 were rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al. (US 5,137,808) in view of Rubenstein (US 5,879,881). In response, Applicants argue that Rubenstein does not teach an affinity binding composition wherein "each receptor type binds specifically to a different protein". Applicants' argumentation is based on the observation that the method of Rubenstein is directed toward detection of different determinants or epitopes of a single antigen, but not multiple antigens. Applicants' argument is fully persuasive and sufficient to overcome these rejections. Accordingly these rejections are withdrawn.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv

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02/04/06